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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/328,632	10/25/94	PORUBEK	D 0204

EXAMINER	
BERCH, M	
ART UNIT	PAPER NUMBER
1202	

12M1/1018

LEGAL AFFAIRS DEPARTMENT
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DATE MAILED: 10/18/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 6/18/96.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7, 9-20 is/are pending in the application.

Of the above, claim(s) 1 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7, 9-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

* U.S GPO: 1996-409-290/40029

Claims 1-7, 9-20 are rejected, 35 USC 112, para 1, for lack of enablement of how to use, for reasons given previously. Note the following:

1. The dosage problem remains, Applicant argues that the second dosage isn't really a daily dosage but the size of a single dose. That is not specifically ~~about~~ what the specification states nor is it consistent with the paragraph as a whole. At the lower end, this would give 0.1 mg/kg a day in 0.001mg/kg doses, i.e. 1000 administrations of a single dose. At the upper end, that translates to 25 administrations of a dose. No one gives a drug 25, or 1000 times a day. Further, the paragraph says the dose is given 1-6 times a day, not 1-25 or 1-1000 times a day. Finally, 10,000 fold ~~a~~ or 40,000 fold dosage ranges is too large to be of any practical value; again. See In re Gardner, 1660 USPQ 138 on this specific point.

2. As stated previously, some choices e.g. XR_5 = alkyl cannot function as ~~producing~~ prodrugs because the body cannot dealkylate an ether.

3. As stated previously, applicants have not presented any evidence that lisofylline has actually been shown useful for anything. Applicants traverse this, but don't go so far as to state what, specifically, lisofylline has been shown useful for. If applicants cannot, who can?

Claims 1-7, 9-20 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Original part 1 remains, no amendment to this point was made.

2. The "naturally occurring" limitation for amino acid does render the term definite. However, three of the amino acid choices in claim 14 (viz, the last 3 species) are not naturally occurring.

3. The expansion of the R_2 and R_3 definition is clearly new matter. That would present for example, ~~R—OH~~ R_2=OH or R_3 = methoxy methoxymethyl. Where is such a choice embraced?

4. Moreover, it isn't enabled. It would for example permit peroxides, e.g. $R_3 = CH_2\ OOCH_3$, which would be too reactive for a pharmaceutical.

5. Original point 4 remains. The term still occurs in claim 1.

6. New claim 20 has N=5-8, i.e. forbids n=4. Hence, this compound cannot function as a prodrug for lisofylline, because it has the wrong size carbon chain

7. In claim 6, "carboxylic acid" has been replaced by "carboxyl alkyl". This is clearly new matter. The group never

has an "alkyl" piece to it; that has been tacked on, and of course its size is unknown.

8. Original point 8 remains. The original questions remain unanswered. It isn't even clear whether the linkage has to be entirely ester e.g. is C(O) O-CH_2-C permitted?

9. Point 9 remains memory the tricycles hardly resolves the problem.

10. The replacement of "acetoxyl" with "acetoxy alkyl" is new matter. While the original term was clearly defective, applicants have not shown support for this particular choice, as opposed to other plausibly choices, such as "C_{1-10} acetylalkyl" or "acetoxy".

11. In claim 1, applicant has deleted unsubstituted C_1 and C_2 alkyl from the Rj definition (now it is C_{3-10}). However, species 10 in claim 14 has $R_5 = CH_3$

12. The three terms added to the third to last line in claim 6 are all new matter. As with point 7 the "alkyl" has appeared from nowhere.

13. Original point 13 remains.

14. Point 14 remains; carbonyl and thiocarbonyl are impractical as substituents.

15. Point 26 remains for the middle 2 terms on page 27, line 33; whereis the CH_3?

16. Point 25 remains. Applicants have cancelled 2 letters from the name, but it is still unclear what this group is. Applicants are ~~argued~~ urged to present a structure in their remarks as to what they think this group is.

17. Point 24 remains. Carbocyclic rings are only permitted 4-7 atoms (see last line of claim 1).

18. Original point 23 remains; these two terms remain

19. original point 19 remains; these terms are still e.g. in claim 6.

20. Point 22 remains. Changing ~~the~~ cyclic to carbocyclic is only a ~~parted~~ partial solution. Thus, does 3-benzoyl propyl qualify? The point of attachment ~~the~~ isn't a carbocyclic atom, but a carbocycle is present.

21. Claim 9 is still broader than claim 1. It refers to "R_1 or R_2", but claim 1 has limited this group to just R2.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-8, 10~~3~~ rejected under 35 U.S.C. § 102(b) as being anticipated by EP 286041.

The reason was given previously. The methoxy group in the reference corresponds in the (claims to R_4 = ~~OX (R_5=H, M=3~~ $OX(R_5)_m$, where X=C R_5= H, m=3.

Claims 1-7, 10, 11, 15-17, 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 93/17684.

The reasons were given previously. Using the broadest possible definition of "substituted.....carbocyclic.....group", the C(OMe)(CF_3)(Ph) group does qualify. It does posses a carbocycle and it is substituted.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claim 20 is rejected under 35 U.S.C. § 103 as being unpatentable over WO 93/17684 or EP 286041.

New claim 20 is restricted to n=5-8, not n=4 of the references. This however is just a chain homolog, a 5 membered chain rather than a 4-membered chain

However, it has been long established that this type of structural relationship-varying the size of a linking carbon

chain - is per se obvious. Specifically, In re Shetty, 195 USPQ 753, In re Wilder, 195 USPQ 426 and Ex Parte Greshem 121 USPQ 422 all feature a compound with a C_2 link rejected over a compound with a C_1 link. In re Chupp, 2 USPQ 2nd 1437 has and In re Coes, 81 USPQ 369 have link unpatentable over a C_2 link Ex parte Ruddy 121 USPQ 427 has a C_3 link unpatentable over a C_1 link Ex parte Nathan, 121 USPQ 349 found the insertion of a C_2H_4 link obvious. In all of these cases, the variation was per-se obvious and did not require a specific teaching. Further, neither reference is limited to just n=4. Alkylene chains are taught generally, and larger chains are specifically seen in EP 286041.

The abstract remains objected to.No indication is given as to use. Moreover, the important Formula II material, in abbreviated term, needs to be present.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE

MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Berch at telephone number (703) 308-4718.

MARK L. BERCH
PRIMARY EXAMINER
GROUP 120 - ART UNIT 1

berch/ds

October 11, 1996